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Psychophysiological Investigations of Patients with Unilateral Symptoms in the Hyperventilation Syndrome

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Anxiety states sometimes lead to hyperventilation (HV) which may, in turn, give rise to a variety of physical symptoms. One way in which HV may present is with unilateral somatosensory symptoms, often left-sided. We report nine such cases. The mechanism of lateralisation was examined using EEG and bilateral somatosensory evoked potentials which were carried out before and after HV. No difference in conduction velocity was found between affected and unaffected arms, but non-specific abnormalities were frequently noted in the EEGs. The results support the role of a central rather than a peripheral mechanism in the production of unilateral symptoms in HV.

Hyperventilation (HV) is defined as a state in which breathing in excess of metabolic requirements leads to hypocapnia. The ability to tolerate HV and the symptoms elicited vary widely (Ames, 1955). HV is often closely associated with psychological disturbance, and the term 'hyperventilation syndrome' (HVS) has been used to describe a symptom complex which arises from the circular relationship between HV and certain psychological states. The psychological component is often neglected because somatic symptoms predominate and, unless the cause is recognised, these patients may be subjected to needless and prolonged intensive physical investigations. Bass & Gardner (1985) have drawn attention to the fact that certain emotional states, particularly phobic and panic disorders, are strongly associated with chronic HVS.

Hyperventilation syndrome may present with unilateral somatic symptoms. This is not often recognised and the mechanism of lateralisation is poorly understood. In one study of the neurological manifestations of HVS, it was found that unilateral paraesthesia was present in 10% of subjects (Perkins & Joseph, 1986). Lateralisation to the left has been reported repeatedly (Lewis, 1953; Blau *et al*, 1983); it has also been reported in other psychological disorders, for example conversion syndromes (Ferenczi, 1926; Galin *et al*, 1977) and hypochondriacal symptoms (Kenyon, 1964). Halliday (1937) found that non-organic, stress-related, rheumatic complaints were frequently left-sided.

Hypotheses that seek to explain not only lateralisation but also the predilection for the left side of the body include both central and peripheral mechanisms. Tavel (1964) favoured a peripheral mechanism on the basis of hemispheric symmetry in the electroencephalograms (EEGs) of both healthy volunteers and subjects with HV. Others attribute the lateralisation of symptoms to physiological changes in the balance of ionised calcium and peripheral blood flow acting on the functional asymmetry of the nerves in the halves of the body (Blau *et al*, 1983). Suggested central mechanisms have included: asymmetrical hypocapnia leading to regional alterations in cerebral blood flow (Coyle & Sterman, 1986); lateralised cerebral specialisation involving mediation of unconscious processes by the right hemisphere (Galin, 1974); anxiety-induced alteration in hemispheric activation (Gruzelier, 1989); and activation of the right hemisphere by stress and emotional arousal (Tucker *et al*, 1977).

In this study we report on patients with unilateral symptoms who were referred for psychiatric assessment and who were subsequently diagnosed as suffering from HVS. In contrast to a previous report of normal EEGs in HVS (Tavel, 1964), it was noted incidentally that some of these patients had non-specific asymmetric abnormalities in routine resting EEGs. We report on the EEG results along with the investigation of peripheral nerve conduction.

Method

Patients with unilateral somatic symptoms reproducible on voluntary HV were considered for inclusion. The diagnosis of HVS was confirmed by measuring end-tidal pCO_2 at rest and under a standard provocation (Gardner & Bass, 1984). An end-tidal pCO_2 of less than 30 mmHg at rest or for a prolonged period after standard provocation is considered to be good laboratory evidence of symptomatic HV. As part of the research protocol each patient had to be free of any major organic illness. As all patients had initially been referred to either cardiologists or neurologists, they had undergone a thorough physical screening before being referred to the psychiatric department. Examination

Table 1
Demographics, diagnoses and results of electroencephalograms of nine patients with HVS

Case no.	Age: years	Sex	Side affected	Duration of complaints: years	Precipitating stressful life events	Diagnosis (DSM-III-R)	Electroencephalogram
1	50	F	Left	11	None	Major depressive episode	Right-sided theta activity; HV - exacerbated slow components
2	39	F	Left	8	Stillbirth	Panic disorder with agoraphobia	Slight asymmetry - slow waves on right side; HV - no change
3	49	M	Left	5	Physical illness	Agoraphobia without panic disorder	Normal at rest; HV produced bilateral theta components
4	36	F	Left	4	None	Somatisation disorder	Normal at rest; HV - diffuse theta wave
5	36	F	Left	4	Assault	Generalised anxiety disorder	Slow waves, more on right side; HV - enhanced slow waves
6	35	F	Right	10	Sexual trauma	Conversion disorder	Mu activity, more on left; HV - enhanced mu
7	44	F	Left	2	Physical illness	Panic disorder without agoraphobia	Left temporal sharp alpha rhythm; HV - increased sharp alpha rhythm
8	31	M	Right	1	Demotion at work	Conversion disorder	Generalised bilateral theta waves; HV - enhanced theta
9	59	M	Left	2	None	Conversion disorder	Normal at rest; HV - no change

and investigations (electrocardiograms, lung function tests, and computerised tomography) excluded neurological and cardiorespiratory pathology.

All patients had a psychiatric assessment. In addition, the Diagnostic Interview Schedule (Robins *et al*, 1985) and the Psychiatric Assessment Schedule (Dean *et al*, 1983) were administered and subjects were then allocated a DSM-III-R diagnosis (American Psychiatric Association, 1987).

Electroencephalograms and nerve conduction studies were performed on all patients who met the inclusion criteria. Nerve conduction studies were performed on both arms by recording somatosensory evoked potentials at three points (Erb's point and at the level of the second cervical vertebra and frontal cortex), giving measures of peripheral and central conduction. Measures taken in the resting state were followed in each case by measures taken during voluntary overbreathing. As far as possible this provocation was continued until the characteristic unilateral symptoms arose, and at that point repeat measures were collected.

Results

Nine patients were identified with symptoms reproducible on HV. Although measurements of end-tidal pCO_2 confirmed the presence of symptomatic HV in only eight of the nine, the remaining patient had so convincingly reproduced her complaints during three minutes of voluntary overbreathing that she was included in the study. All were right-handed according to the Annett questionnaire (Annett, 1970).

Six patients had originally been referred to a neurologist, and three to a cardiologist. Six were women (Table 1). Mean age at the time of psychiatric assessment was 42 years and mean duration of symptoms was five years. Epilepsy-like seizures accompanied the somatosensory complaints in five patients and two of these (cases 1 and 2) had previously been prescribed anticonvulsants, with little therapeutic effect. In six patients a stressful life event had precipitated the syndrome.

Four patients had no overt mood disturbance but instead manifested psychological distress physically. The other five had both anxiety and depressive symptoms, with anxious

Table 2
Mean (s.d.) scores for evoked potential conduction velocity (ms) before and after hyperventilation on affected and unaffected arms ($n = 6$)

Site	Affected		Unaffected	
	Before HV	After HV	Before HV	After HV
Erb's point	9.2 (0.5)	9.3 (0.7)	9.2 (0.8)	9.2 (0.7)
Second cervical vertebra	13.6 (0.9)	13.6 (0.8)	13.8 (1.3)	13.9 (1.3)
Frontal cortex	19.3 (1.3)	19.3 (1.3)	19.2 (1.6)	19.1 (1.9)

No significant differences were found.

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mood and panic attacks being the predominant clinical features. Only one patient had pronounced depressive symptoms. Diagnoses according to DSM-III-R are given in Table 1.

The EEG results were normal in three patients, revealed non-specific, asymmetrical abnormalities in the contralateral hemisphere in two and in the ipsilateral hemisphere in three, and there were bilateral slow waves while alert in one (χ^2 was non-significant). HV produced an exacerbation of the non-specific asymmetrical abnormalities in five patients, caused no further change in one, and produced slow waves in two of the three with normal resting EEGs (the latter is considered a normal manifestation of HV).

While recording the somatosensory evoked potentials, six patients successfully produced unilateral symptoms on HV; the other three failed to do so. Table 2 shows the means and standard deviations of the evoked potentials of these six. There were no significant differences in recordings on the affected limb (*t*-tests) before and after HV, nor any significant differences after HV between affected and unaffected limbs (*t*-tests). Even though the number tested was small, the measurements showed little variance.

Discussion

In terms of personal characteristics, this sample resembles HVS cases described in previous studies (Ames, 1955; Dolle, 1964; Weimann, 1968). There was a predominance of women, an age range of 31–59, a high incidence of preceding stressful life events, and a tendency to present to hospital physicians. The presence of neurotic symptoms in general, and phobic and panic symptoms in particular, are also in keeping with other studies (Compernolle *et al*, 1979; Garssen *et al*, 1983). Individual susceptibility to overbreathing varies (Garssen, 1980), and stress can trigger HV (Grossman *et al*, 1985). Patients under stress may be in a hyperadrenergic state which can cause HV by β-adrenergic overstimulation (Margarian, 1982). In some cases the tendency to overbreathe persists even when the stress has passed (Garssen, 1980).

Many of the diverse somatic symptoms associated with HV are explicable in terms of the physiological changes it induces. As the alveolar and arterial pCO_2 falls, the pH of the blood and cerebrospinal fluid increases. Acidic metabolites accumulate and there is an alteration in the intra/extracellular balance of calcium ions. Kugelberg (1948) claimed that there is an increase in excitability of the peripheral nerves, the vulnerability of the various fibres depending both on size and on movement of calcium into the fibre. In one study a central reduction in cerebral blood flow was found (Woolman *et al*, 1968) and others claim an increase in the excitability of most of the cerebral neurons during hyperventilation (Speckman & Caspers, 1973). Garssen (1986) suggests that a more generalised neuronal excitability arises. Physiological changes certainly contribute to our understanding of the diversity of symptoms produced by HV. However, they do not explain why lateralised sensorimotor symptoms arise, and in particular why these tend to occur on the left side of the body.

The peripheral theory favoured by Tavel (1964) and Blau *et al* (1983), which proposes that the natural asymmetry of peripheral nerves and their nutrient vessels in the halves of the body is responsible for lateralisation of symptoms, is not supported by the lack of change in conduction velocity in the affected limbs after HV. Our results before and after HV showed little variance. However, the number tested was small and evoked potentials might not be sensitive enough to detect a change.

Unilateral slow waves are unusual in healthy adults, but a mild to moderate excess of generalised slow waves during wakefulness is found in 10–15% of normal adults (Spehlmann, 1981). The EEG response to HV normally involves the development of generalised slow waves. However, it is abnormal for the slow waves of HV to be asymmetrical or focal in distribution (Spehlmann, 1981).

The findings of non-specific abnormalities in two-thirds of this case series at rest, with an enhancement during HV in five out of six cases, suggest a central mechanism in the production of lateralised somatosensory symptoms in HVS. A variety of neurotic disorders have been linked with HVS. Ferenczi (1926) hypothesised that the right cerebral hemisphere was involved in the mediation of unconscious phenomena. Galin (1974) linked the right hemisphere with psychic processes and proposed that psychosomatic symptoms, being the expression of the right hemisphere, would be more likely to appear on the left side of the body. Empirical studies have found activation of the right hemisphere during stress and emotional arousal (Tucker *et al*, 1977). The right hemisphere may play a specific role in stress and emotional disorders, and this may be a manifestation of cerebral dominance (Galaburda *et al*, 1978). Further testing using neuropsychological techniques and electrodermal habituation (Gruzelier, 1989) may clarify the underlying mechanism.

In summary, the results of this small, uncontrolled study favour a central rather than a peripheral mechanism in the production of lateralised somatosensory symptoms in HVS. This is supported by previous reports implicating involvement of the right hemisphere in stress and emotional arousal, features shared by many in this group of patients. However, further investigation is needed.

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